

## News Release

### Title

**Elucidation of new therapeutic strategies in locally advanced pancreatic head cancer  
~Usefulness of neoadjuvant chemoradiotherapy~**

### Key Points

○Neoadjuvant chemoradiotherapy followed by surgery was found to improve the long-term survival rate in patients with pancreatic head cancer involving exclusively the portal vein system and that abutting the major artery.

○Neoadjuvant chemoradiotherapy was found to reduce the incidence of pathologically positive lymph node metastasis and positive dissected peripancreatic tissue margin.

### Summary

Dr. Tsutomu Fujii and Prof. Yasuhiro Kodera (Department of Gastroenterological Surgery (Surgery II) in Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.) demonstrated that neoadjuvant chemoradiotherapy (NACRT) rather than upfront surgery improved long-term survival in pancreatic head cancer involving the surrounding blood vessels.

Pancreatic cancer has been increasing year by year in Japan, and often in progress at the time of diagnosis with involvement of the surrounding blood vessels, such as the portal vein or the superior mesenteric artery. Upfront surgery had been considered to be the best option; however, recurrence rate was extremely high, and the development of new treatment strategy has been urgently necessary. This is the collaborative study with Dr. Sohei Satoi and Prof. Masanori Kon (Department of Surgery) in Kansai Medical University, and a total of 504 patients treated with curative intent for pancreatic head cancer were analyzed. In patients with pancreatic head cancer without vascular involvement, long-term survival was equivalent between the upfront surgery group and the NACRT group. In patients with pancreatic head cancer involving exclusively the portal vein system and that abutting the major artery, NACRT followed by surgery was found to improve the long-term survival rate. NACRT was found to reduce the incidence of pathologically positive lymph node metastasis and positive dissected peripancreatic tissue margin, suggesting that it may contribute the better survival. Recently, intensive new chemotherapy has become available, and this study is expected to become an important opportunity for the improvement of long-term outcome of pancreatic cancer patients. This work was published online in Journal of Gastroenterology on May 11, 2016.

## **Research Background**

Pancreatic cancer is the fourth leading cause of cancer-related death worldwide and has the worst prognosis, with only 3% of patients surviving for 5 years after diagnosis. The efficacy of neoadjuvant chemoradiotherapy (NACRT) and subset of pancreatic cancer patients who are most likely to benefit from this strategy remain elusive. The aim of this collaborative study with Kansai Medical University was to investigate the effects of NACRT, and a total of 504 patients treated with curative intent for pancreatic head cancer were analyzed. We classified three categories according to the NCCN guidelines as below; 1) resectable, 2) borderline resectable involving exclusively the portal vein system, and 3) borderline resectable abutting the major artery. Inverse probability of treatment weighting analysis was used to reduce the impact of treatment-selection bias and the potential confounding factors inherent to an observational study.

## **Research Results**

Four hundred sixteen patients underwent upfront surgery, and 88 patients underwent NACRT. The NACRT regimen consisted of radiation therapy (50.4 gray in 28 fractions) combined with systemic chemotherapy involving oral S-1, the oral 5-fluorouracil pro-drug tegafur with oteracil and gimeracil. S-1 was orally administered twice daily (80 mg/m<sup>2</sup>/day) from days 1 to 14 and from days 22 to 35. In patients with resectable pancreatic cancer without vascular invasion, 2-year survival rate was statistically equivalent between the upfront surgery group and the NACRT group (52.2% vs 59.2%, respectively) after propensity score matching. However, in patients with borderline resectable pancreatic cancer involving exclusively the portal vein system, the estimated 2-year survival was significantly longer in the NACRT group than in the the upfront surgery group (71.1% vs 25.6%, respectively). Moreover, the estimated 2-year survival was significantly longer in the NACRT group than in the the upfront surgery group (38.4% vs 15.4%, respectively) in patients with borderline resectable pancreatic cancer abutting the major artery. Regressions weighted by propensity scores revealed that no significant differences in the operative blood loss, blood loss volume, or postoperative hospital stay in the NACRT patients with lesions with vascular invasion. NACRT was found to reduce the incidence of pathologically positive lymph node metastasis and positive dissected peripancreatic tissue margin, suggesting that it may contribute the better survival.

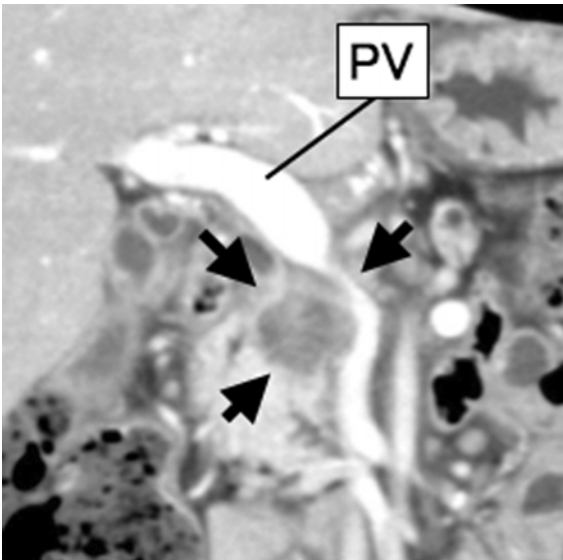


Figure 1. Pancreatic head cancer involving the portal vein (PV) (Coronal plane CT)

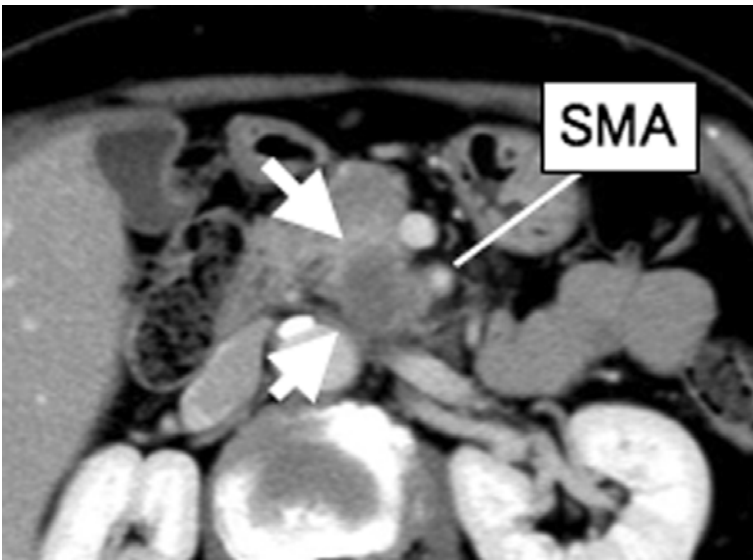


Figure 2. Pancreatic head cancer abutting the superior mesenteric artery (SMA) (Axial plane CT)

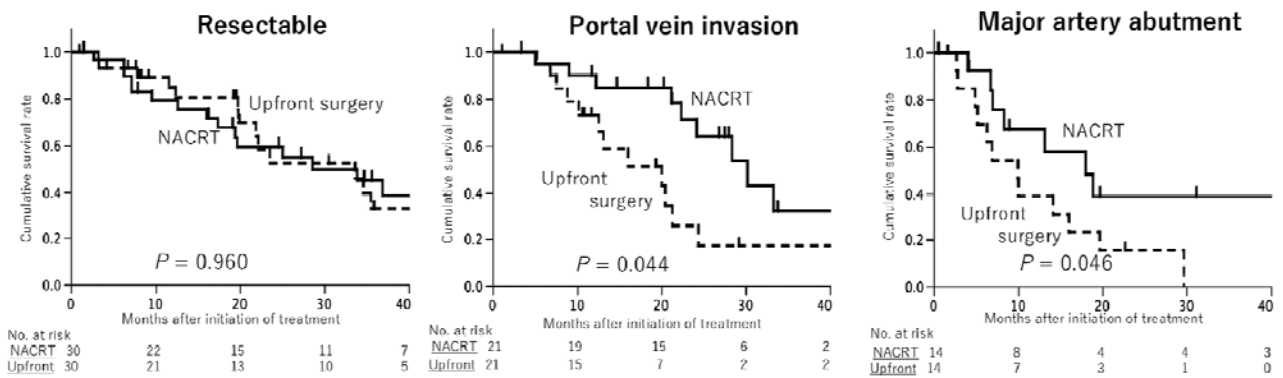


Figure 3. Overall survival of the upfront surgery group and the NACRT group

## **Research Summary and Future Perspective**

Recently, intensive new chemotherapy has become available. These findings suggest that NACRT rather than upfront surgery offers clinical benefits to patients with borderline resectable adenocarcinoma of the pancreatic head with vascular involvement. This study is expected to become an important opportunity for the improvement of long-term outcome of pancreatic cancer patients.

## **Publication**

Tsutomu Fujii, Sohei Satoi, Suguru Yamada, Kenta Murotani, Hiroaki Yanagimoto, Hideki Takami, Tomohisa Yamamoto, Mitsuro Kanda, So Yamaki, Satoshi Hirooka, Masanori Kon, and Yasuhiro Kodera.

Clinical Benefits of Neoadjuvant Chemoradiotherapy for Adenocarcinoma of the Pancreatic Head: An Observational Study using Inverse Probability of Treatment Weighting.

*Journal of Gastroenterology*, May, 11, 2016.

## **Japanese ver.**

[http://www.med.nagoya-u.ac.jp/medical/dbps\\_data/material/nu\\_medical/res/topix/2016/nacrt\\_20160518jp.pdf](http://www.med.nagoya-u.ac.jp/medical/dbps_data/material/nu_medical/res/topix/2016/nacrt_20160518jp.pdf)